# CLAIMS

We claim

1. A substrate for hybridization comprising a plurality of first nucleic acid alone or in combination with a plurality of one or more oligomers that are not nucleic acids immobilized on at least a portion of the substrate in a medium-high or high immobilization density

2. The substrate of claim 1 wherein a second nucleic acid having a region of contiguous nucleotides that are complementary to all or part of at least one of the first nucleic acids will selectively hybridize to the at least one first nucleic acid.

3. The substrate of claim 2 wherein, in an assay, the difference in $T_m$ between

   - (i) a fully-matched complex immobilized to the substrate, the complex comprising the first nucleic acid and the second nucleic acid; and

   - (ii) a mismatched complex immobilized to the substrate, the complex comprising the first nucleic acid and a second nucleic acid having a single nucleotide mismatch;

   is not decreased compared to the difference in $T_m$ between the complexes in low immobilization density.

4. The substrate of claim 3 wherein difference in $T_m$ between (i) and (ii) is increased compared to the difference in $T_m$ between the complexes in low immobilization density.

5. The substrate of claim 4 wherein the difference in $T_m$ is at least 5 degrees Celsius.

6. The substrate of any of claims 1 to 5, wherein the medium-high immobilization density comprises oligomers on the substrate so that the ratio ($r_s$) of the mean centre-to-centre separation distance of the oligomers to the average length of immobilized oligomers is less than or equal to 2.

7. The substrate of claim 1 wherein the high immobilization density comprises oligomers on the substrate so that the ratio ($r_s$) of the mean centre-to-centre separation distance of the oligomers to the average length of immobilized oligomers less than or equal to 1.7

8. The substrate of claim 1 wherein the nucleic acid is a dendritic assembly containing nucleic acid residues.

9. The substrate of claim 1 wherein the first nucleic acids are immobilized to the substrate by a linker.

10. The substrate of claim 9 wherein the linker comprises a polyether moiety, a poly(ethylene oxide) moiety or a polymeric moiety.

11. The substrate of claim 1 wherein the one or more oligomers other than nucleic acids are immobilized to the substrate by a linker.

12. The substrate of claim 11 wherein the linker comprises a polyether moiety, a poly(ethylene oxide) moiety or a polymeric moiety.

13. The substrate of claim 1 wherein the first nucleic acids comprise identical nucleic acid sequence.

14. The substrate of claim 1 wherein the first nucleic acids comprise a mixture of nucleic acid sequences.

15. The substrate of claim 1 wherein the first nucleic acids comprise a mixture of nucleic acid sequences and/or nucleic acid analogues and/or nucleotide analogue sequences.

16. A substrate of claim1 wherein a plurality of first nucleic acids and a plurality of one or more oligomers that are not nucleic acids are immobilized on the substrate.

17. The substrate of claim 1, wherein the one or more oligomers comprise polyelectrolyte moieties and/or polymeric moieties.

18. The substrate of claim 1 wherein the one or more oligomers are polyethers.

19. The substrate of claim 1 wherein the second nucleic acid and the at least one first nucleic acid hybridize in a high ionic strength solution.

20. The substrate of claim 18 wherein the high ionic strength solution is at least 0.3 mol/L.

21. The substrate of claim 1 wherein the interfacial hybridization for fully complementary nucleic acids exhibits enhanced sensitivity to temperature

22. The substrate of claim 1wherein the substrate comprises an optical fiber, an optical wave-guide, a spot on a microarray chip, a microtiter plate well, a metal film for surface plasmon resonance determination, a glass bead, a planar waveguide, a quartz oscillator, a ceramic oscillator, a conductive electrode material, a semi-conductive electrode material, a plastic sample compartment, an optical component or a pyroelectric material.

23. The substrate of claim 1 which is a substrate for a hybridization assay.

24. The substrate of claim 1 further comprising a plurality of first nucleic acids alone or in combination with a plurality of one or more oligomers that are not nucleic acids immobilized on at least a portion of the substrate in a low immobilization density.

25. A method of preparing a substrate for hybridization, comprising immobilizing a plurality of first nucleic acids alone or in combination with one or more oligomers that are not nucleic acids to the substrate in a medium-high or high immobilization density.

26. The method of preparing a substrate for hybridization of claim 25 comprising immobilizing a plurality of first nucleic acids to the substrate alone or in combination with one or more oligomers that are not nucleic acids in a high immobilization density.

27. The method of claim 25 wherein the nucleic acids are a dendritic assembly containing nucleic acid residues.

28. The method of claim 25 wherein the first nucleic acids are connected to the substrate by a linker.

29. The method of claim 28 wherein the linker comprises a polyether moiety, a poly(ethylene oxide) moiety or a oligomer moiety.

30. The method of claim 25 wherein the first nucleic acids comprise an identical nucleic acid sequence.

31. The method of claim 25 wherein the first nucleic acids comprise a mixture of nucleic acid sequences.

32. The method of claim 25 wherein the substrate comprises an optical fiber, an optical wave-guide, a spot on a microarray chip, a microtiter plate well, a metal film for surface plasmon resonance determination, a planar waveguide, a quartz oscillator, a ceramic oscillator, a conductive electrode material, a semi-conductive electrode material, a glass bead, a plastic sample compartment, an optical component or a pyroelectric material.

33. A method of hybridizing nucleic acids comprising:

- providing a substrate including a plurality of first nucleic acids or first nucleic acids and oligomers which are not nucleic acids on the substrate, having a medium-high or high immobilization density; and
- contacting the substrate with at least one second nucleic acid having a region of contiguous nucleotides that are complementary to all or part at least one of the first nucleic acids, so that the second nucleic acid hybridizes to the at least one first nucleic acid.

34. The method of claim 33, wherein the second nucleic acid selectively hybridizes to the at least one first nucleic acid.

35. The method of claim 33 wherein, in an assay, the difference in $T_m$ between

- (i) a fully-matched complex immobilized to a substrate, the complex comprising the first nucleic acid and the second nucleic acid; and

- (ii) a mismatch complex immobilized to a substrate, the complex comprising the first nucleic acid and a second nucleic acid having a single nucleotide mismatch;

is increased or maintained relative to the difference in $T_m$ between the complexes in low immobilization density.

36. The method of claim 35, wherein the difference in $T_m$ is at least 5 degrees Celsius.

37. The method any of claims 33 wherein the second nucleic acid and the at least one first nucleic acid hybridize in a high ionic strength solution.

38. The method of claim 37 wherein the high ionic strength solution is at least 0.3 mol/L.

39. The method of claim 33 wherein the hybridization comprises a $T_m$ inversion effect.

40. The method of claim 33 wherein the hybridization for fully complementary nucleic acids exhibits enhanced sensitivity to temperature

41. The method of claim 33 wherein the first nucleic acids comprise an identical nucleic acid sequence.

42. The method of claim 33 wherein the first nucleic acids comprise a mixture of nucleic acid sequences.

43. The method of claim 33 wherein the first nucleic acids comprise a mixture of nucleic acid sequences.

44. The method of claim 33 wherein the substrate comprises an optical fiber, an optical waveguide, a spot on a microarray chip, a microtiter plate well, a metal film for surface plasmon resonance determination, a planar waveguide, a quartz oscillator, a ceramic oscillator, a conductive electrode material, a semi-conductive electrode material, a glass bead, a plastic sample compartment, an optical component or a pyroelectric material.

45. The method of claim 33 wherein the substrate is contacted with a mixture of nucleic acids including the at least one second nucleic acid.

46. The method of claim 33further comprising a step of detecting hybridization.

47. The method of claim 46 wherein hybridization is detected by detection of fluorescence.

48. A method of detecting the presence of a genetic target in a test sample, comprising:

- providing a substrate including a plurality of genetic marker nucleic acids immobilized to the substrate, alone or in combination with one or more oligomers at a medium-high or high immobilization density;

- contacting the substrate with a test sample comprising a mixture of nucleic acids so that a second nucleic acid having a region of contiguous nucleotides that are complementary to all or part of at least one of the genetic marker nucleic acids hybridizes to at least one first nucleic acid; and

- detecting hybridization of the genetic marker to the second nucleic acid, wherein hybridization is indicative of the presence of a genetic target in the sample.

49. The method of claim 48, wherein the second nucleic acid selectively hybridizes to the at least one genetic marker nucleic acid.

50. The method of claim 48 wherein, in an assay, the difference in $T_m$ between

- (i) a fully-matched complex immobilized to a substrate, the complex comprising the first nucleic acid and the second nucleic acid; and

- (ii) a mismatch complex immobilized to a substrate, the complex comprising the first nucleic acid and a second nucleic acid having a single nucleotide mismatch;

is increased or maintained relative to the difference in $T_m$ between the complexes in low immobilization density.

51. The method of claim 48 wherein the difference in $T_m$ is at least 5 degrees Celsius.

52. The method of any of claims 47-50 wherein the hybridization comprises a $T_m$ inversion effect.

53. The method of claim 48 wherein the second nucleic acid and the at least one first nucleic acid hybridize in a high ionic strength solution.

54. The method of claim 53 wherein the high ionic strength solution is at least 0.3 mol/L.

55. The method of claim 48 wherein the hybridization for fully complementary nucleic acids exhibits enhanced sensitivity to temperature

56. The method of claim 48 wherein the first nucleic acids comprise an identical nucleic acid sequence.

57. The method of claim 48 wherein the first nucleic acids comprise a mixture of nucleic acid sequences.

58. The method of claim 48 wherein the first nucleic acids comprise a mixture of nucleic acid sequences.

59. The method of claim 48 wherein the substrate comprises an optical fiber, an optical waveguide, a spot on a microarray chip, a microtiter plate well, a metal film for surface plasmon resonance determination a planar waveguide, a quartz oscillator, a ceramic oscillator, a conductive electrode material, a semi-conductive electrode material, a glass bead, a plastic sample compartment, an optical component or a pyroelectric material.

60. The method of claim 48 wherein the genetic target comprises a disease marker nucleic acid and wherein hybridization is indicative of the presence of a disease state in the subject sample.

61. The method of claim 48 wherein the test sample comprises a sample obtained from a patient or derived from nucleic acids obtained from a patient.

62. The method of claim 48 wherein the nucleic acids are derived by a nucleic acid amplification method.

63. The method of claim 48 wherein the genetic target comprises an environmental marker nucleic acid, a food marker nucleic acid or a biowarfare agent nucleic acid, and wherein hybridization is indicative of the presence of the genetic target in the sample.

64. The method of claim 48 wherein the test sample comprises a sample obtained from an environmental source, food source, patient source or derived from one of the aforementioned sources.

65. The method of claim 48 wherein the nucleic acids to be tested are derived by a nucleic acid amplification method.

66. The method of claim 48 wherein hybridization of the marker to the second nucleic acid is detected with an indicator agent that indicates hybridization of the marker to the second nucleic molecule.

67. The method of claim 48wherein the nucleic acids to be tested comprise an indicator agent.

68. The method of claim 67 wherein the indicator agent comprises a fluorophore.

69. The method of claim 33 wherein the hybridization is conducted below the $T_m$ of a complex of the first nucleic acid and second nucleic acid but above the $T_m$ of a complex of the a first nucleic acid and a complementary nucleic acid having a single nucleotide mismatch.

70. The method of claim 48 wherein the hybridization is conducted below the $T_m$ of a complex of the first nucleic acid and second nucleic acid but above the $T_m$ of a complex of the a first nucleic acid and a complementary nucleic acid having a single nucleotide mismatch.

71. The use of the substrate of claim 1 for diagnosing a disease state or detecting a genetic target.

72. A kit for detecting the presence of a genetic target in a test sample, comprising one or more substrates of any of claim 1.

73. The kit of claim 72 further comprising a hybridization buffer.

74. The kit of claim 72 wherein the genetic target comprises a disease marker nucleic acid, an environmental marker nucleic acid, a food marker nucleic acid or a biowarfare agent nucleic acid.

75.A method for identifying or isolating a target nucleic acid from a mixture containing nucleic acids which comprises the steps of:

providing a substrate of claim 1 wherein the first nucleic acids comprise a sequence that is complementary at least in part to the target nucleic acid; and

contacting the substrate with the mixture containing nucleic acids such that any target nucleic acid present in the mixture can hybridize to the first nucleic acids on the substrate.

76.The method of claim 75 wherein the step of contacting the substrate with the mixture is performed at high ionic strength.

77.The method of claim 75 wherein the mixture containing nucleic acids can contain nucleic acids that differ from the target nucleic acid by a single base change.